Empirical / pre-emptive antifungal therapy in adult neutropenic patients

Click here for clinical pathway

Definitions

**Empirical** antifungal therapy: use of antifungals in a neutropenic patient with persisting fever of unknown source despite empirical antibacterial therapy and in the absence of supporting evidence of invasive fungal infection.

**Pre-emptive** antifungal therapy: use of antifungals in a neutropenic patient with persisting fever despite empirical antibacterial therapy and in the presence of evidence suggestive of invasive fungal infection.

Rationale

Recent evidence and guidance supports the use of pre-emptive antifungal therapy in preference to routine use of empirical antifungal therapy in this setting. Empirical antifungal therapy is generally not advised for patients with an anticipated duration of neutropenia < 10 days.

This flow chart can be used at any time in the management of a neutropenic patient. Typically it will be used in patients with ongoing fever and clinical concern at day 5 review of empirical antibacterial therapy

(See Neutropenic Sepsis - Empirical Antibacterial Therapy Protocol)

Symptoms and signs suggesting possible mucormycosis?

- e.g. evidence of sinusitis, palatal necrosis, nasal discharge, periorbital oedema/cellulitis, proptosis?

![Flow Chart]

Yes

send cultures if possible

discuss with haematologist / oncologist / microbiologist, ENT surgeon and radiologist

start iv Ambisome® 5 mg/kg/day

Review Ambisome® therapy based on investigation results

haematologist / oncologist and microbiologist decide to commence or defer antifungal therapy

**Note:** Typical CT chest abnormality (eg halo sign, air crescent, cavitation) OR Positive aspergillus galactomannan result OR fungal hyphae seen or cultured from sputum / BAL. is sufficient evidence to commence pre-emptive antifungal therapy

Defer antifungals

Commence antifungals

1st line – voriconazole

(300mg bd)

Either: iv 4 mg/kg bd (iv if seriously ill) OR po 200mg bd* (300mg bd* if necessary)

2nd line – micafungin

iv 100mg od*

3rd line - Ambisome®

iv 3 mg/kg/day

Salvage therapy: discuss apparent treatment failure with microbiologist, consider serum voriconazole levels if relevant

**Note 1:** Micafungin may be 1st choice in suspected candidiasis

Note2: previous antifungal prophylaxis and potential drug interactions may affect choice of agent *dose reduction if pt <40kg, see BNF

Frequent clinical review

Consider repeat investigations as above; if results suggest fungal infection commence antifungals

Consider antifungal therapy if ongoing clinical concern and risk factors e.g. neutropenia / GVHD

Oral switch therapy and treatment duration is assessed on a case by case basis but general principles include:

- Continuation of antifungal therapy until up to 3 days after resolution of profound neutropenia i.e. neutrophils >0.5 x 10^9/l.
- Consider oral switch therapy to po voriconazole 200 mg every 12 hours if patient clinically responding and able to tolerate and absorb oral medication.
- Check with pharmacist that drug interactions do not preclude voriconazole therapy.
- Posaconazole may be an alternative oral switch therapy in patients unable to tolerate voriconazole
- Results from large clinical trials of empirical antifungal therapy in febrile neutropenics demonstrate a median treatment duration of approximately 10 days. Duration of pre-emptive antifungal therapy is likely to be longer than this because the probability of invasive fungal infection is greater.